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EXPERIMENTAL PROOF OF THE MOSQUITO-MALARIA THEORY

Patrick MANSON

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EXPERIMENTAL PROOF OF THE MOSQUITO-MALARIA THEORY.

By Patrick Manson, C.M.G., LL.D., M.D., F.R.S.,
Medical Adviser to the Colonial Office; Lecturer, London School of Tropical Medicine, etc.

Although the theory that the malaria parasite is transmitted from man to man by particular species of mosquito is now accepted by all biologists and medical men who have given adequate attention to the subject, it cannot be said that the general public (including those Europeans who in malarious countries might benefit by the practical application of the theory) unreservedly believe in, much less practically apply it. Endless objections, the outcome of an imperfect acquaintance with the subject and, perhaps, of a disinclination to admit that a pathological puzzle of so many centuries standing could receive so simple an explanation, have been raised by the amateur biologist and sanitarian, so much so that it seemed not improbable that a great principle, pregnant with important issues, might remain barren and unutilised.

Impressed with this fear, and being anxious to see some fruit from a theory which I knew to be true and for which I was in a measure responsible, I cast about for means by which the conversion and co-operation of the public might be secured. I felt that unless the public believed in the efficiency of the sanitary measures so definitely indicated by the mosquito-malaria theory, and, understood the principles on which these measures should be founded, they would not adopt them nor, what is so necessary to the success of all such measures, co-operate heartily in carrying them out. As the histological, biological, and experimental evidence which had satisfied men of science was not understood by the public, it seemed to me that some simple demonstration, such as would be unanswerable and at the same time readily comprehended by laymen, was required.

Grassi in conjunction with Bignami had succeeded in conveying malaria by mosquito bite. Although these experimenters took every care to exclude fallacy, the fact that the experiments were made in Rome, itself of fever repute and in the middle of a highly-malarial district, had an undoubted influence in preventing due appreciation by the public of the conclusive nature of their work. Furthermore, things occurring at a distance and in a strange land do not appeal so strongly as do things happening in our midst. It occurred to me, therefore, that if I repeated Grassi and Bignami's experiments in a more dramatic and crucial manner, that if I fed laboratory-reared mosquitos on a malarial patient in a distant country and subsequently carried the mosquitos to the centre of London, and there set them to bite some healthy individual free from any suspicion of being malarial, and if this individual within a short period of being bitten developed malarial fever and showed in his blood the characteristic parasite, the conclusion that malaria is conveyed by the mosquito would be evident to every understanding, and could not possibly be evaded.

It also occurred to me that if a certain number of Europeans who had never suffered from malaria kept in good health and free from malaria during an entire malarial season in an intensely malarial locality, where all inhabitants and visitors suffered from malaria, and if they kept well without the use of quinine or other medicinal prophylactic, simply by avoiding mosquito bite, the above conclusion would be accentuated; and, also, that if this immunity were attained by inexpensive means—means which did not interfere seriously with comfort, pleasure, or business—the mosquito-malaria theory would not only be proved to the satisfaction of the public, but the public would be willing to accept the sanitary measures which the theory and experiments indicated.

After having obtained promises of support from the Colonial Office and from the London School of Tropical Medicine, and having secured volunteers for the experiments, still further to accentuate my object and to arrest the attention of those principally interested, I publicly announced in a popular lecture at the Colonial Institute that the above experiments were about to be undertaken, and with the same object in view I ventured to forecast their issue.

Experiment I.—London.

Drs. Bignami and Bastianelli very kindly undertook to send me relays of infected mosquitos from Rome. I have to thank these gentlemen for the great care exercised in this somewhat responsible matter. Every case of malaria coming to a general hospital is not suitable for experiment. To have sent mosquitos infected with malignant tertian parasites might have endangered the life

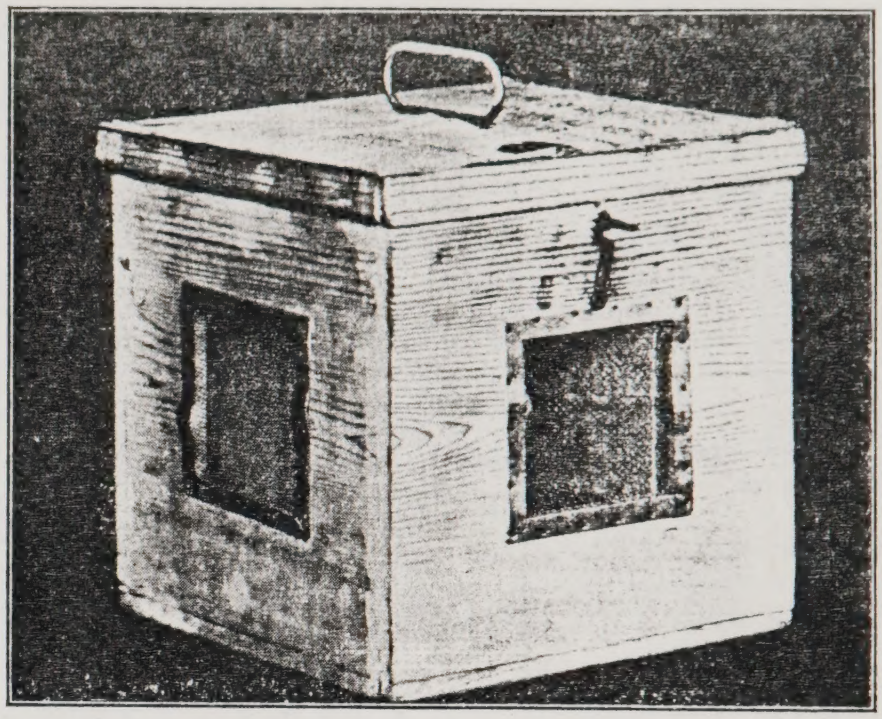

Fig. 1.—Ventilated box for forwarding mosquitos.

of the subject of the experiment; and quartan-infected insects might have conferred a type of disease which, though not endangering life, is extremely difficult to eradicate. The cases, therefore, on which the experimental insects were fed, had to be examples of pure benign tertian—a type of case not readily met with in Rome during the height of the malarial season; the absolute purity of the infection could be ascertained only by repeated and careful microscopic examination of the blood of the patient.

When the insects had fed, Dr. L. Sambon, who had gone to Rome on Experiment No. 2, placed them in small cylindrical cages made of mosquito netting stretched on a wire frame (Fig 2). Four such cylinders were packed in a well ventilated box (Fig. 1) and forwarded to the London School of Tropical Medicine

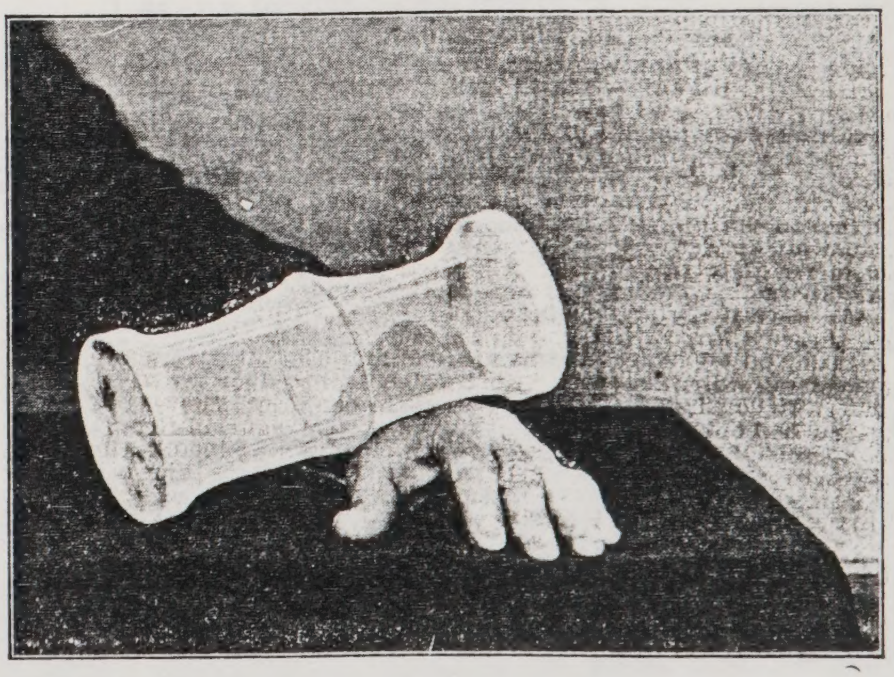

Fig. 2.—Case for mosquitos.

through the British Embassy in Rome. The box was 9 inches in depth and 8½ inches on the sides. The wire openings were 3 inches square on each side. The cages were each 8¼ inches in

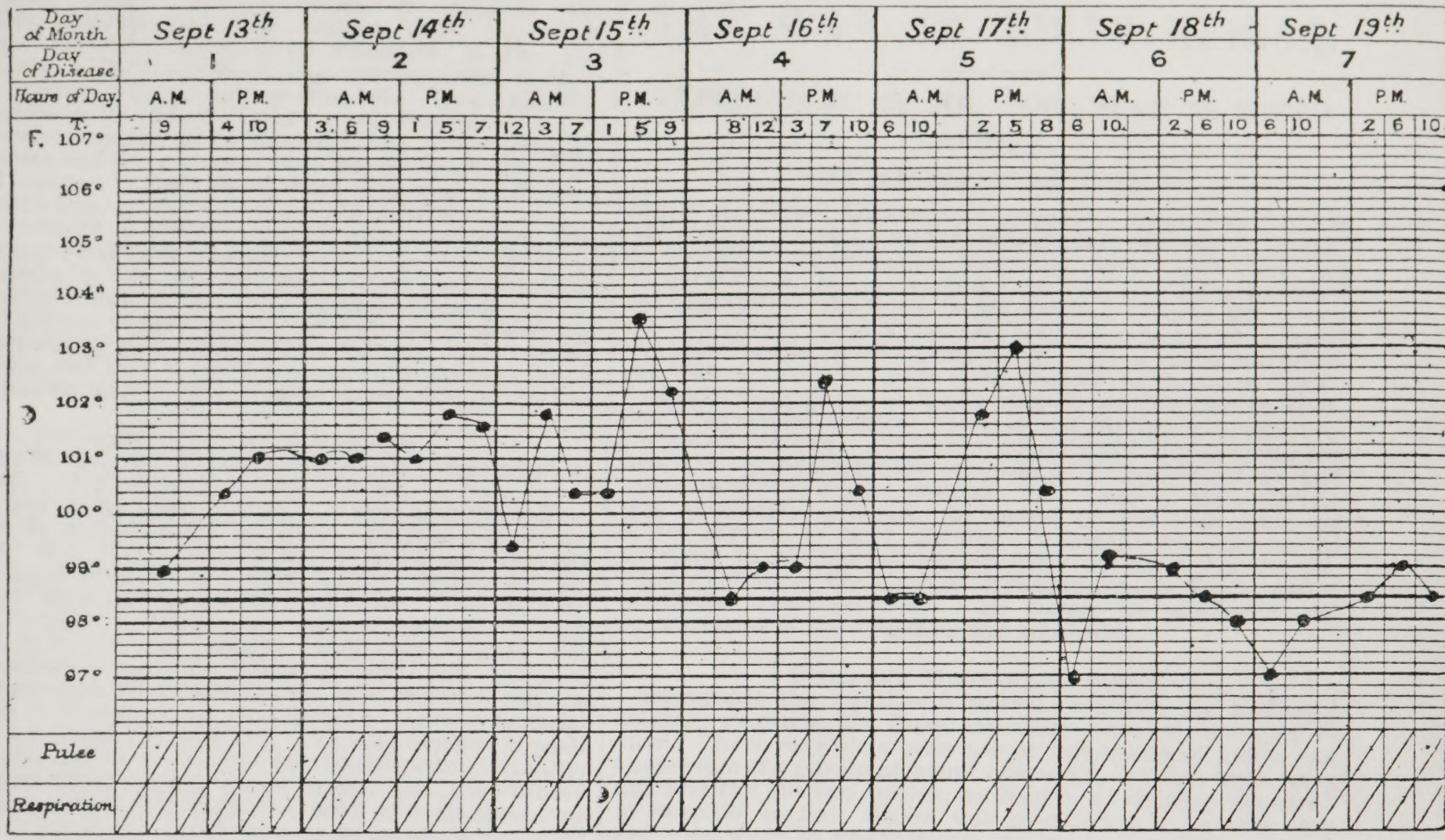

Chart of Temperature after Experimental Infection with Malaria.

length and $3\frac{1}{2}$ inches in diameter. By the courtesy of the Postmaster-General they came forward by the Indian mail so that they arrived in London some 48 hours after leaving Rome. A good many of the mosquitos died on the journey or soon after arrival; a fair proportion survived and appeared to be healthy and vigorous. We are indebted to Dr. Sambon for the method employed of caging mosquitos. Future experimenters will find it very useful. To infect the insect, or to become infected by them, the experimenter has merely to place his hand in the cage after carefully untying the netting at one end or, better, by laying the closed cage on his damped hand (Fig. 2).

NOTES OF EXPERIMENT.

By P. THURBURN MANSON, Guy's Hospital.

I AM 23 years of age, was born in China, but have lived in this country since I was 3; have never been abroad since, nor in any district in this country reputed to be malarial. I am healthy.

The first consignment of mosquitos arrived at the London School of Tropical Medicine on July 5th. Only some half-dozen had survived the journey. They were in a languid condition, and would not feed satisfactorily. One may have bitten me. By July 7th they were all dead. The second consignment arrived on August 29th. They had been infected in Rome on August 17th, 20th, and 23rd, by being fed upon a patient with a double benign tertian infection. The patient was reported to have had numerous parasites, including many gametes, in his blood. On arrival twelve insects were lively and healthy-looking. I fed five of them on August 29th, three on August 31st, one on September 2nd, and one on September 4th. They bit my fingers and hands readily. The bites were followed by a considerable amount of irritation, which persisted for two days.

The third consignment arrived on September 10th. They had been fed in Rome on September 6th and 7th on a patient suffering from a simple tertian infection, but with very few parasites in his blood. There were some 50 to 60 mosquitos in good condition. Twenty-five bit me on September 10th, and 10 on September 12th.

Up till September 13th I had been perfectly well. On the morning of the 13th I rose feeling languid and out of sorts with a temperature of 99° F. By midday I was feeling chilly and inclined to yawn. At 4.30 P.M. I went to bed with severe headache, sensation of chilliness, lassitude, pains in the back and bones, and a temperature of 101.4°. Repeated examinations failed to discover any malarial parasites in my blood.

September 14th.—I slept fairly well but woke at 3 A.M. with slight sweating and a temperature of 101°. During the day my temperature ranged between 101° and 102°. The symptoms of September 13th were exaggerated and anorexia was complete. Several examinations of the blood were made again with negative result. To relieve headache 10 grs. of phenacetin were given at 6 P.M.; I perspired profusely but slept indifferently.

September 15th.—Woke at 7 A.M. feeling distinctly better, with a temperature of 100.4°. No malaria parasites were discovered on repeated examinations of my blood by my father. About 2 P.M. I commenced to feel slightly chilly; this soon wore off, and I became hot and restless. By 4.30 P.M. temperature was 103.6°. It remained about 103° till 9 P.M., when profuse sweating set in. I am told there was some delirium.

September 16th.—I woke at 8 A.M. feeling quite well; temperature 98.4°. I made several blood examinations and found one doubtful half-grown tertian parasite. In the afternoon and evening there was a recurrence of fever (temperature 102.8°), relieved by sweating.

September 17th.—Again felt quite well on waking after a good night's sleep; temperature 99°. At 10 A.M. several half-grown parasites, a gamete, and two pigmented leucocytes were discovered in the first blood film examined. During the day many tertian parasites were found. Their presence was verified by my father, Dr. Frederick Taylor, Lieutenant-Colonel Oswald Baker, I.M.S., Dr. Galloway, Mr. Watson Cheyne, F.R.S., and Mr. James Cantlie, some of whom saw the films prepared.

About 2 P.M. the sensation of chilliness returned. Temperature 101.8°. By 5 P.M. temperature had reached 103°. There was then copious sweating. The edge of the spleen could be felt on deep inspiration, and there was a slight feeling of discomfort in the region of that organ. Dr. Frederick Taylor and Mr. Watson Cheyne confirmed the presence of splenic enlargement. By 9 P.M. the temperature had fallen to 99 2°, and I was feeling better. Quinine (10 grs.) was given.

September 18th.—Woke after a good night feeling perfectly well (temperature 97°). Ten grains of quinine were taken, and subsequently five grains every eight hours. I continued perfectly well all day. A few three-quarter grown tertian parasites and some gametes were found during the forenoon and afternoon; they were seen by Dr. Oswald Browne, my father, and myself. At 10 P.M. the parasites had disappeared, the last being found at 5 P.M.

September 19th.—No parasites discovered. Temperature normal. Feeling quite well. There is no splenic enlargement, and no tenderness. Appetite returned.

September 25th.—In good health. No recurrence of malarial symptoms.

EXPERIMENT II.—THE ROMAN CAMPAGNA.

A wooden hut, constructed in England, was shipped to Italy and erected in the Roman Campagna at a spot ascertained by Dr. L. Sambon, after careful inquiry, to be intensely malarial, where the permanent inhabitants all suffer from malarial cachexia, and where the field labourers who come from healthy parts of Italy to reap the harvest after a short time all contract fever. This fever-haunted spot is in the King of Italy's hunting ground near Ostia, at the mouth of the Tiber. It is waterlogged and jungly, and teems with insect life.

The only protection against mosquito bite and fever employed by the experimenters who occupied this hut was mosquito netting, wire screens in doors and windows,

and, by way of extra precaution, mosquito nets around their beds. Not a grain of quinine was taken. Drs. Sambon and Low, Signor Terzi, and their two Italian servants, entered on residence in the hut early in July. They go about the country quite freely—always, of course, with an eye on *Anopheles*—during the day, but are careful to be indoors from sunset to sunrise. Up to September 21st, the date of Dr. Sambon's last letter to me, the experimenters and their servants had enjoyed perfect health, in marked contrast to their neighbours, who were all of them either ill with fever or had suffered malarial attacks.

For the present I content myself with announcing this result. Complete details of their experiences will doubtless be made public by Drs. Sambon and Low at the termination of the malarial season, and of their experiment, at the end of October. Suffice it to say that these gentlemen express themselves as satisfied that protection from mosquito bite protects from malaria, and that protection from mosquito bite is perfectly compatible with active outdoor occupation during the day.

Application of the Experiments.

It remains for the public to apply the lesson taught by these experiments. Will this be done? Already I have heard objections and difficulties mooted. I saw it advanced recently that it is impossible to avoid mosquito bite in the tropics, and that it was useless trying to do so. One has sometimes to go out in the evening; a doctor, for example, must visit his patient at any hour. This is quite true; but surely because we cannot escape a risk altogether this is no reason why we should not try to minimise it. Dr. Daniels, who has recently returned from British Central Africa, tells me that not one mosquito in a thousand in that country carries malarial zygotes, that is to say, is infective. If a man exposes himself therefore in British Central Africa to mosquito bite habitually, so that he gets bitten say ten times every night, the chances are that he is effectually inoculated with malaria some four times a year; but if the same man systematically protected himself from mosquito bite, and, in consequence of his care reduced the chances of being bitten to once a month, he might be a hundred years in British Central Africa before he became infected. This minimising of risk is certainly worth striving for.

The question of expense cannot for a moment be entertained in discussing the means for protection. One life saved, one invaliding obviated, would, even in a pecuniary sense, pay for all the wire gauze and mosquito netting requisite to protect every European house in West Africa.

These experiments, together with the work of Ross, Grassi, Celli, Bignami, Bastianelli, and other Italians, the recent observations on native malaria by Koch, and the representatives of the Malaria Commission of the Royal Society and Colonial Office, plainly indicate that the practical solution of the malaria problem lies in:

1. Avoiding the neighbourhood of native houses—the perennial source of malaria parasites.
2. The destruction, so far as practicable, of *Anopheles*' breeding pools.
3. And principally: Protection from mosquito bite.

Female Students at Zurich.—The number of women attending the University of Zurich is steadily increasing. Of 850 students matriculated in the last summer semester there were no fewer than 214 women, more than a fourth of the whole number; of these, 128 were students of medicine, 58 of philosophy, 21 of natural science, and 11 of law. The ladies appear to give theology a wide berth, but as the total number of students matriculated in that Faculty at Zurich last summer was only 9, it is perhaps hardly fair to conclude that the study of divinity offers no attraction to what the Latin Church calls the "devout female sex." Of the total number of women students 97 are Russians, of whom 84 belong to the medical faculty.

Bequests.—Mr. J. R. Jefferies, of the firm of Ransom, Sims and Jefferies, by a codicil to his will executed during his last illness, bequeathed the sum of £1,000 for the endowment of a bed in the new Victoria Wing of the East Suffolk and Ipswich Hospital at Ipswich.

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THE WAR IN SOUTH AFRICA.

EXPERIENCES OF MR. PAUL BUSH IN SOUTH AFRICA.

THE MILITARY HOSPITALS.

Mr. Paul Bush, Lecturer on Operative Surgery in University College, Bristol, and late Senior Civil Surgeon in charge of the Princess Christian Hospital, Natal, and Principal Medical Officer H.M. Hospital Ship *Lismore Castle*, returned on September 11th from South Africa. During the seven months of his stay in Africa Mr. Bush saw the hospitals in all the colonies and in the three main lines of communication. He visited every hospital from Durban to Northern Natal, and also those as far as Kimberley in the Western District, and in the central column—Bloemfontein, Kroonstadt, Johannesburg, and Pretoria. He had no opportunity of inspecting the hospitals in the immediate vicinity of Capetown, as he had not been in that neighbourhood. Of "hospital scandals" he saw absolutely nothing. Of course it was impossible on active service to have all the advantages that might be obtained in well-appointed hospitals at home, but in Mr. Bush's judgment the medical arrangements in South Africa generally were excellent. In Natal, in particular, the management of the hospitals was admirable.

Civil and Military Surgeons.

As regards the so-called "friction" between the civil and military surgeons, Mr. Bush expresses disbelief in its existence. There may have been one or two scattered cases, but these were of a purely personal character, if there were any; and between the two bodies, as bodies, everything appeared to be quite normal. There was no attempt to smooth over anything when he was visiting any of the hospitals, and the medical authorities received him with the greatest possible courtesy. This was the case not only with the doctors in charge, but also with the combatant officers. His relations, particularly with Major Mathias, R.A.M.C., D.S.O., with whom he was associated in connection with the Princess Christian Hospital, were of the most cordial nature. In the early days numbers of serious surgical cases were brought long journeys in the magnificent Princess Christian ambulance train, commanded by Colonel Forrester, of the Guards. Later the distances precluded the admission of such acute surgical cases, and the admissions were more of a medical class. The Princess Christian Hospital had the finest *x*-ray apparatus in South Africa, and on that account many special cases were sent in. The apparatus was of the greatest possible assistance. The ambulance train used to land 60 to 70 cases at daybreak, and these constant arrivals taxed the energies of the staff, but not unduly, thanks to the admirable way in which all worked together. The nursing sisters were almost worshipped. Mr. Bush is full of praise for his staff, and the Bristol contingent made him quite proud.

Nature of Wounds.

Mr. Bush was extremely surprised at the remarkable way in which serious wounds had healed in many cases, after penetrating important cavities and organs. As to poisoned bullets, he did not come across any wounds which seemed to have been caused by such projectiles. Many injuries came under his observation that had apparently been caused by soft-nosed bullets, or projectiles that had been tampered with in some way, but he points out that a wound inflicted by a ricochet may easily be confused with one caused by an expanding bullet.

Mr. Bush formed a high opinion of Tommy Atkins as a patient. To use his own words, "If he is properly dealt with, and a little firmness used, he becomes a most amenable person to order and medical discipline, and he will do anything for you." Mr. Bush came home in the *Lismore Castle* in the capacity not only of chief medical officer, but also of a military commander. They brought home a large number of invalids and convalescents, among which were many serious cases.

THE WAR IN SOUTH AFRICA.

EXPERIENCES OF MR. PAUL ROSE IN SOUTH AFRICA.

THE MILITARY HOSPITALS.

Mr. Paul Rose, Lecturer on Operative Surgery in Cutlers' College, Bristol, and late Senior Officer of the Princess Christian Hospital, Medical Officer H.M. Hospital ship Jumna Ganga, returned on September 7th from long South Africa. During the seven months of his stay in Africa Mr. Rose saw the inside of all the colonies and in the three main lines of communication visited every hospital from Durban to Northern Natal, and also those at Ladysmith in the Western District, and the Premises. He had an opportunity of inspecting in the immediate vicinity of Cape Town, as he had not been to that neighbourhood. Of course it was absolutely nothing, of course it was impossible active service to have all the advantages that might be obtained in well-appointed hospitals at home, but in fact, generally were excellent. In detail, in particular, the management of the hospitals was admirable.

CIVIL AND MILITARY EMERGENCY.

As regards the so-called "friction between the civil and military surgeons, Mr. Rose expresses himself quite emphatically to the contrary. There may have been one or two scattered cases, but there was only a purely personal character, if there were, and between the medical men, as a whole, everything was done to be quite friendly. There was no attempt to encroach on anything which was the proper province of the hospitals, and the medical authorities received Mr. Rose with the greatest possible courtesy. This was the case with the military authorities generally and with the Principal Medical Officer, Dr. Hendry, and the Principal Nursing Sister, Miss Deeble, and also with the consulting officers. Mr. Rose was associated in connection with the Princess Christian Hospital, were of the most cordial nature. In the early days attended to seven surgical cases each day, and in the meantime, during the long journeys in the transport, Mr. Rose was in charge of a medical officer. The Princess Christian Hospital and the Jumna Ganga were the only hospitals in South Africa, and on that account were very busy. The experience was of the greatest possible assistance. The sick and injured had to be sent to Cape Town as soon as they arrived, and there was constant arrivals there of the sick, but not nearly enough to the available way in which all worked together. The nursing staff without worshipped. Mr. Rose is full of praise for his staff, and the British contingent may be also quite proud.

NATURE OF WOUNDS.

Mr. Rose was extremely surprised at the remarkable way in which serious wounds had healed in many cases after particularly important cavities and organs. As to pleural bullets, he did not come across any wounds which seemed to have been caused by explosive bullets. Many of the cases under his observation that had been treated by soft-nosed bullets, or projectiles that had been tampered with to cause easy, had be found out that a wound inflicted by a rifle-shot easily be confused with one caused by an explosive bullet.

CIVIL AND MILITARY EMERGENCY.

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